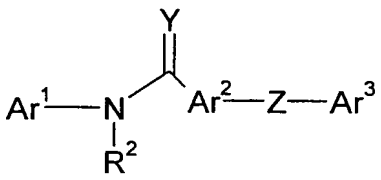
Patent Claims

1. Compounds of the formula I



I

in which

Ar^1, Ar^2, Ar^3 each, independently of one another, denote an aromatic radical or Het, each of which is unsubstituted or mono-, di- or polysubstituted by R^1,

Het denotes a mono- or bicyclic aromatic heterocycle having 1, 2, 3 or 4 N, O and/or S atoms,

R^1 in each case, independently, denotes H, A, aryl, OR^4, SR^4, Oaryl, Saryl, $N(R^4)_2$, NHaryl, Hal, NO_2, CN, $(CH_2)_mCOOR^4$, $(CH_2)_mCOOaryl$, $(CH_2)_mCON(R^4)_2$, $(CH_2)_mCONHaryl$, COR^4, COaryl, $S(O)_mA$, $S(O)_maryl$, NHCOA, NHCOaryl, $NHSO_2A$, $NHSO_2aryl$ or $SO_2N(R^4)_2$, $O(CH_2)_n N(R^4)_2$, $O(CH_2)_nNHR_3$, $O(CH_2)_nNH_2$, $O(CH_2)_n$-morpholine, $O(CH_2)_n$-piperazine, $O(CH_2)_n$-pyrrolidine, $O(CH_2)_n$-piperidine, O-piperidine, $O(CH_2)_n$-oxopiperazine, $O(CH_2)_n$-oxomorpholine, $O(CH_2)_n$-oxopyrrolidine, $O(CH_2)_nC(CH_3)_2(CH_2)_nN(R^4)_2$, $N(CH_2)_nC(CH_3)_2(CH_2)_nN(R^4)_2$, $O(CH_2)_nN(R^4)SO_mA$, $O(CH_2)_nN(R^4)SO_mN(R^4)A$, $O(CH_2)_nN(R^4)SO_maryl$, $(CH_2)_nN(R^4)SO_mA$, $(CH_2)_nN(R^4)SO_mN(R^4)A$, $(CH_2)_nN(R^4)SO_maryl$, $O(CH_2)_nSO_mA$, $O(CH_2)_nSO_mN(R^4)A$,

$O(CH_2)_nSO_maryl$, $(CH_2)_nSO_mA$, $(CH_2)_nSO_mN(R^4)A$ and/or $(CH_2)_nSO_maryl$,

Y denotes O, S, C-NO_2, $C(CN)_2$ or N-R^3,

Z denotes $G^1{}_n$, $G^1{}_nEG^2{}_m$, $EG^1{}_nG^2{}_m$ or $G^1{}_nG^2{}_mE$,

R^2, R^3, R^4 each, independently of one another, denote H, A or -alkylene-aryl,

A denotes unbranched or branched alkyl having 1-10 C atoms, in which one or two CH_2 groups may be replaced by O or S atoms and/or by -CH=CH- groups and/or also 1-7 H atoms may be replaced by Hal,

aryl denotes phenyl which is unsubstituted or mono-, di- or polysubstituted by A, phenyl, OA, SA, Ophenyl, NH_2, NA_2, Hal, NO_2, CN, $(CH_2)_mCOOR^4$, $(CH_2)_mCON(R^4)_2$, COR^4, COaryl, $S(O)_mA$, NHCOA or NHSO2A,

E denotes O, SO_m, NR^1, CO, C=N or alkene,

G^1, G^2 each, independently of one another, denote CR^1R^1 or E,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2, 3, 4 or 5,

m denotes 0, 1 or 2,

and pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1 in which

Ar^1 denotes phenyl which is mono- or disubstituted by R^1,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2 in which

Ar^2 denotes unsubstituted phenyl,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1 to 3 in which

Ar^3 denotes pyridinyl which is monosubstituted by R^1,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1 to 4 in which

Y denotes O or S,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1 to 5 in which

Z denotes O or CR^1R^1,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to one or more of Claims 1 to 6 in which

R^2 denotes H,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to one or more of Claims 1 to 7 in which

R^1 in each case, independently, denotes H, A, Hal, OH, OA, CF_3 and/or CONHA,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

9. Compounds according to Claim 1 in which

Ar^1	denotes phenyl which is mono- or disubstituted by R^1,
Ar^2	denotes unsubstituted phenyl,
Ar^3	denotes pyridinyl which is monosubstituted by R^1,
Y	denotes O or S,
Z	denotes O or CR^1R^1,
R^2	denotes H,
R^1	in each case, independently, denotes H, A, Hal, OH, OA, CF_3 and/or CONHA,

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

10. Compounds according to Claim 1 selected from the group

a) N-methyl-4-[3-(2-hydroxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

b) N-methyl-4-[4-(2-hydroxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

c) N-methyl-4-[3-(2-hydroxy-5-methylphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

d) N-methyl-4-[4-(2-hydroxy-5-methylphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

e) N-methyl-4-[4-(2-hydroxy-4-methylphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

f) N-methyl-4-[3-(4-fluoro-2-hydroxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

g) N-methyl-4-[3-(5-chloro-2-hydroxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

h) N-methyl-4-[3-(4-chloro-2-hydroxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

i) N-methyl-4-[3-(2,5-dimethoxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

j) N-methyl-4-[3-(5-chloro-2-methoxyphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

k) N-methyl-4-[3-(5-tert-butyl-2-hydroxyphenylcarbamoyl)phenoxy]-pyridine-2-carboxamide

l) N-methyl-4-[3-(hydroxytrifluoromethylphenylcarbamoyl)phenoxy]-pyridine-2-carboxamide

m) N-methyl-4-[3-(2-methoxy-5-trifluoromethylphenylcarbamoyl)-phenoxy]pyridine-2-carboxamide

n) N-methyl-4-[3-(5-ethanesulfonyl-2-hydroxyphenylcarbamoyl)-phenoxy]pyridine-2-carboxamide

o) N-methyl-4-{3-[2-(2-dimethylaminoethoxy)-5-trifluoromethylphenylcarbamoyl]phenoxy}pyridine-2-carboxamide

p) N-methyl-4-[3-(2-methoxy-5-trifluoromethylphenylcarbamoyl)-phenoxy]pyridine-2-carboxamide

q) N-methyl-4-[3-(3-trifluoromethanesulfonylphenylcarbamoyl)-phenoxy]pyridine-2-carboxamide

r) N-methyl-4-[3-(1H-indazol-7-ylcarbamoyl)phenoxy]pyridine-2-carboxamide

s) N-methyl-4-[3-(1H-indol-7-ylcarbamoyl)phenoxy]pyridine-2-carboxamide

t) N-methyl-4-[3-(5-bromo-1H-indol-7-ylcarbamoyl)phenoxy]pyridine-2-carboxamide

u) N-methyl-4-[3-(5-tert-butyl-2-methoxyphenylcarbamoyl)phenoxy]-pyridine-2-carboxamide

v) N-methyl-4-[3-(3-trifluoromethylphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

w) N-methyl-4-[3-(4-trifluoromethylphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

x) N-methyl-4-[3-(2-methoxy-5-methylphenylcarbamoyl)phenoxy]pyridine-2-carboxamide

y) N-methyl-4-[3-(3-chloro-4-fluorophenylcarbamoyl)phenoxy]pyridine-2-carboxamide

z) N-methyl-4-[3-(3-chlorophenylcarbamoyl)phenoxy]pyridine-2-carboxamide

aa) N-methyl-4-[3-(4-fluoro-3-trifluoromethylphenylcarbamoyl)-phenoxy]pyridine-2- carboxamide

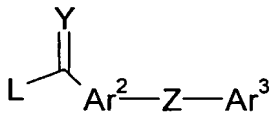
bb) N-methyl-4-[3-(3-fluoro-4-trifluoromethylphenylcarbamoyl)-phenoxy]pyridine-2-carboxamide

and the pharmaceutically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios.

11. Process for the preparation of compounds of the formula I and physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, characterised in that a compound of the formula II

II

in which Ar^1 and R^2 have the meanings indicated in Claim 1, is reacted with a compound of the formula III



III

in which Y, Ar^2, Z and Ar^3 have the meanings indicated in Claim 1 and

L denotes Cl, Br, I or a free or reactively functionally modified OH group,

and/or a base or acid of the formula I is converted into one of its salts.

12. Medicaments comprising at least one compound according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

13. Medicaments comprising at least one compound according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

14. Set (kit) consisting of separate packs of

a) an effective amount of a compound according to one or more of Claims 1 to 10 and/or physiologically acceptable derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, and

b) an effective amount of a further medicament active ingredient.

15. Compounds according to one or more of Claims 1 to 10 and physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, as activators or inhibitors of kinases.

16. Compounds according to one or more of Claims 1 to 10 and physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, as inhibitors of tyrosine kinases and/or of Raf kinases.

17. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of diseases.

18. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of diseases that are caused, mediated and/or propagated by kinases and/or by kinase-mediated signal transduction.

19. Use according to Claim 18, where the kinases are selected from the group of the tyrosine kinases.

20. Use according to Claim 19, where the tyrosine kinases are TIE-2 or VEGFR.

21. Use according to Claim 18, where the kinases are selected from the group of the Raf kinases.

22. Use according to Claim 21, where the Raf kinases are A-Raf, B-Raf or Raf-1.

23. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of solid tumours.

24. Use according to Claim 23, where the solid tumour is selected from the group consisting of brain tumour, tumour of the urogenital tract, tumour of the lymphatic system, stomach tumour, laryngeal tumour and lung tumour.

25. Use according to Claim 23, where the solid tumour is selected from the group consisting of monocytic leukaemia, lung adenocarcinoma, small cell lung carcinomas, pancreatic cancer, glioblastomas and breast carcinoma.

26. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of diseases that are caused, mediated and/or propagated by angiogenesis.

27. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisom-

ers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of diseases selected from the group consisting of retinal vascularisation, diabetic retinopathy, age-induced macular degeneration and/or inflammatory diseases.

28. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of bone pathologies selected from the group consisting of osteosarcoma, osteoarthritis and rickets.

29. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of diseases selected from the group consisting of psoriasis, rheumatoid arthritis, contact dermatitis, delayed hypersensitivity reaction, inflammation, endometriosis, scarring, benign prostatic hyperplasia, immunological diseases, autoimmune diseases and immunodeficiency diseases.

30. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts, derivatives, solvates and stereoisomers thereof, including mixtures thereof in all ratios, for the preparation of a medicament for the treatment and/or prophylaxis of diseases selected from the group consisting of brain cancer, lung cancer, squamous cell cancer, bladder cancer, gastric cancer, pancreatic cancer, hepatic cancer, renal cancer, colorectal cancer, breast cancer, head cancer, neck cancer, oesophageal cancer, gynaecological cancer, thyroid cancer, lymphoma, chronic leukaemia and acute leukaemia.

31. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment and/or prophylaxis of diseases, where a therapeutically effective amount of a compound according to one or more of Claims 1 to 10 is administered in combination with a compound from the group 1) oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitors, 7) HMG-CoA reductase inhibitors, 8) HIV protease inhibitors 9) reverse transcriptase inhibitors, 10) growth factor receptor inhibitors and 11) angiogenesis inhibitors.

32. Use of compounds according to one or more of Claims 1 to 10 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment and/or prophylaxis of diseases, where a therapeutically effective amount of a compound according to one or more of Claims 1 to 10 is administered in combination with radiotherapy and a compound from the group 1) oestrogen receptor modulator, 2) androgen receptor modulator, 3) retinoid receptor modulator, 4) cytotoxic agent, 5) antiproliferative agent, 6) prenyl-protein transferase inhibitors, 7) HMG-CoA reductase inhibitors, 8) HIV protease inhibitors, 9) reverse transcriptase inhibitors, 10) growth factor receptor inhibitors and 11) angiogenesis inhibitors.